

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>66777</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/ 01032</b>	International filing date (day/month/year) <b>14/01/2000</b>	(Earliest) Priority Date (day/month/year) <b>22/01/1999</b>
Applicant  <b>THE GOVERNEMENT OF THE UNITED STATES OF AMERICA as</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

**METHODS FOR THE PREVENTION AND TREATMENT OF DISEASES CAUSED BY AN INFLAMMATORY RESPONSE MEDIATED BY ENDOGENOUS SUBSTANCE P BY USING ANTI-SUBSTANCE P ANTIBODIES**

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

/US 00/01032

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K39/395 A61P1/00 A61P11/00 A61P19/00 A61P31/00  
 A61P37/00 //C07K7/22

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>A. JAFARIAN ET AL.: "Passive immunization with an anti-substance P antibody prevents substance P- and neurokinin A-induced bronchospasm in anesthetized guinea pigs." LIFE SCIENCES, vol. 57, no. 2, 1995, pages 143-153, XP000914597 Oxford, GB cited in the application abstract</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	<p>1,2,5,6, 9,10,13, 14,19, 20,23, 24,27, 28,31,32</p>

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

8 June 2000

Date of mailing of the international search report

29/06/2000

Name and mailing address of the ISA

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Nooij, F

## INTERNATIONAL SEARCH REPORT

International Application No

P US 00/01032

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	A. AGRO ET AL.: "Inhibition of murine intestinal inflammation by anti-substance P antibody." REGIONAL IMMUNOLOGY, vol. 5, no. 2, March 1993 (1993-03), pages 120-126, XP000914600 New York, NY, USA abstract ----	1,2,5,6, 9,10,13, 14,19, 20,23, 24,27, 28,31,32
X	P. PICCIOLI ET AL.: "Neuroantibodies: ectopic expression of a recombinant anti-substance P antibody in the central nervous system of transgenic mice." NEURON, vol. 15, no. 2, August 1995 (1995-08), pages 373-384, XP000914598 Cambridge, MA, USA cited in the application abstract ----	1,5,9, 13,14, 19,23, 27,31,32
A	WO 92 16547 A (CHILDRENS MEDICAL CENTER) 1 October 1992 (1992-10-01) the whole document ----	1-36
A	WO 96 29326 A (GLAXO GROUP LTD.) 26 September 1996 (1996-09-26) the whole document ----	1-36
T	R. TRIPP ET AL.: "Respiratory syncytial virus infection and G and/or SH protein expression contribute to substance P, which mediates inflammation and enhanced pulmonary disease in BALB/c mice." JOURNAL OF VIROLOGY, vol. 74, no. 4, February 2000 (2000-02), pages 1614-1622, XP002139777 Baltimore, MD, USA the whole document -----	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

US 00/01032

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9216547	A	01-10-1992	NONE		
WO 9629326	A	26-09-1996	AU	5333596 A	08-10-1996
			EP	0815104 A	07-01-1998
			JP	11502810 T	09-03-1999
			US	5919803 A	06-07-1999
			ZA	9602200 A	30-10-1996

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference <b>66777</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US00/01032</b>	International filing date (day/month/year) <b>14/01/2000</b>	Priority date (day/month/year) <b>22/01/1999</b>
International Patent Classification (IPC) or national classification and IPC <b>A61K39/395</b>		
Applicant <b>THE GOVERNEMENT OF THE UNITED STATES OF AMERICA as</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 8 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  <b>25/07/2000</b>	Date of completion of this report  <b>28.03.2001</b>
Name and mailing address of the international preliminary examining authority:   <b>European Patent Office</b> <b>D-80298 Munich</b> <b>Tel. +49 89 2399 - 0 Tx: 523656 epmu d</b> <b>Fax: +49 89 2399 - 4465</b>	Authorized officer  <b>Barz, W</b>  Telephone No. <b>+49 89 2399 7320</b>



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/01032

## I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

### Description, pages:

1-32 as originally filed

### Claims, No.:

1-36 as originally filed

### Drawings, sheets:

1/3-3/3 as originally filed

### Sequence listing part of the description, pages:

1 page, filed with the letter of 03.05.00

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/01032

- ☐ the description,      pages:
- ☐ the claims,      Nos.:
- ☐ the drawings,      sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-36 (IA).

because:

- ☒ the said international application, or the said claims Nos. 1-36 (IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/01032

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## 1. Statement

Novelty (N)	Yes:	Claims	2-4, 6-18, 21-22, 24-36
	No:	Claims	1, 5, 19-20, 23
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-36
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims	

## 2. Citations and explanations see separate sheet

## VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**



**ITEM III:**

**Claims 1-36** relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT). See, however, item V-3. below.

**ITEM V:**

Reference is made to the following documents:

D1: LIFE SCIENCES, vol. 57, 1995, pages 143-153, (JAFARIAN A. et al.);  
cited in the application;

D2: REGIONAL IMMUNOLOGY, vol. 5, 1993, pages 120-126, (AGRO A. et al.);

**1. NOVELTY**

**Claims 1, 5, 19-20, and 23** do not meet the requirements of Article 33(2) PCT for the following reasons:

- 1.1 A method for treating a disease in a subject, said method comprising all the features of **claim 1** of the present application, is disclosed in document D2 (abstract; page 123, left column, last paragraph; page 124, left column, last paragraph; page 124, left column, lines 23-28; figure 6). Therefore, the subject-matter of claim 1 is not novel in the sense of Article 33(2) PCT.
- 1.2 The dependent **claim 5** is also not new, because D2 also discloses the administration of anti-substance P antibodies (abstract).
- 1.3 A method for preventing a disease (asthma) in a subject, said method comprising all the features of **claim 19** of the present application, is disclosed in document D1 (abstract; page 148, last paragraph; page 149, first paragraph; page 151, last 5 lines; page 152, lines 3-5 and last paragraph; figures 4-5). Therefore, the subject-matter of claim 19 is not novel in the sense of Article 33(2) PCT.

1.4 The dependent **claims 20 and 23** are also not new, because:

- the prevention of asthma (in guinea-pigs) is also disclosed in D1 (abstract);
- the administration of anti-substance P antibodies to the subject is also known from D1 (abstract).

1.5 The remaining **claims 2-4, 6-18, 21-22, and 24-36** appear to be novel, because none of the available prior art documents discloses the same combination of features as in these claims.

## 2. INVENTIVE STEP

However, **claims 2-4, 6-18, 21-22, and 24-36** do not appear to be inventive (Article 33(3) PCT) for the following reasons:

2.1 Compared to document D2, which is considered to represent the closest prior art for claims 1-18, the subject-matter of **claim 2** differs only in the disease or syndrome to be treated. However, said diseases and syndromes are merely some of several straightforward possibilities which the skilled person knows as diseases caused by inflammatory responses. Similar arguments apply to the subject-matter of **claims 3-4**. Consequently, the subject-matter of claims 2-4 also lacks an inventive step.

2.2 The dependent **claims 6-18** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT with respect to inventive step, the reasons being as follows:

- The administration of anti-substance P antibodies (claims 6-8) is also known from D2 (abstract);
- It is generally known to the skilled person that antibody fragments have binding features equivalent to those of intact antibodies and can thus be interchanged with intact antibodies where circumstances make it desirable, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of claims 9-12 also appears to lack an inventive step;

- The range of concentrations claimed in claims 13-18 also cannot be regarded as inventive, because said concentrations do not appear to result in any unexpected effects, but seem to fall within the scope of the customary practice followed by skilled persons.

2.3 The dependent **claims 21-22 and 24-36** do not appear to meet the requirements of Article 33(3) PCT for the same reasons as outlined in item V-2.2 above.

### 3. INDUSTRIAL APPLICABILITY

For the assessment of **claims 1-36** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

#### **ITEM VII:**

1. The amino acid sequence of substance P (SEQ ID NO:1) listed on page 3, line 4, of the description and in the sequence listing is not consistent with the sequence of substance P in the prior art, because the order of the amino acids is inverted.
2. Figure 3 is not clear, because the labelling of its horizontal axis ("CA") is not consistent with the description ("LPS" on page 11, line 11).
3. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D2 is not mentioned in the description, nor is this document identified therein.
4. Vague and not precisely defined expressions related to the "spirit" of the invention (page 24, line 28, and page 31, line 27) are unallowable (PCT Guidelines III-4.3a).

5. The incorporation of disclosures by reference (see page 32, lines 10-13) is not allowed (PCT Guidelines II-4.17).

**ITEM VIII:**

1. **Claims 1 and 19** are not clear (Article 6 PCT), because it is not apparent to which term (method, disease, subject?) the expression "which is caused by an inflammatory response to the disease or syndrome" refers.
2. **Claims 2 and 20** are not clear in the sense of Article 6 PCT, because the "rejection of allografts and other transplanted tissues or organs" does not fall under the term "disease or syndrome". Furthermore, this feature is not referred to in the description. Therefore, claims 2 and 20 are also not supported by the description as required by Article 6 PCT.
3. **Claim 3** is not clear (Article 6 PCT), because it refers to the "infection" of claim 1, although claim 1 does not mention any "infection". An analogous objection applies to **claim 21**, which refers to the "infection" of claim 19.